

Treatment of Chronic Pain with Cannabidiol (CBD) and Tetrahydrocannabinol (THC)

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University of Utah

Time Line of Regulatory Approvals

IND Approval

- September 6th, 2017

IRB Approval

- September 18th, 2017

Certificate of Confidentiality Approval

- October 3rd, 2017

Schedule I Registration Approval

- January 12th, 2018

Study Drug Received

- January 11th, 2019

IRB Post IND Compliance Audit

- May 9th, 2019

Study Design



Testing



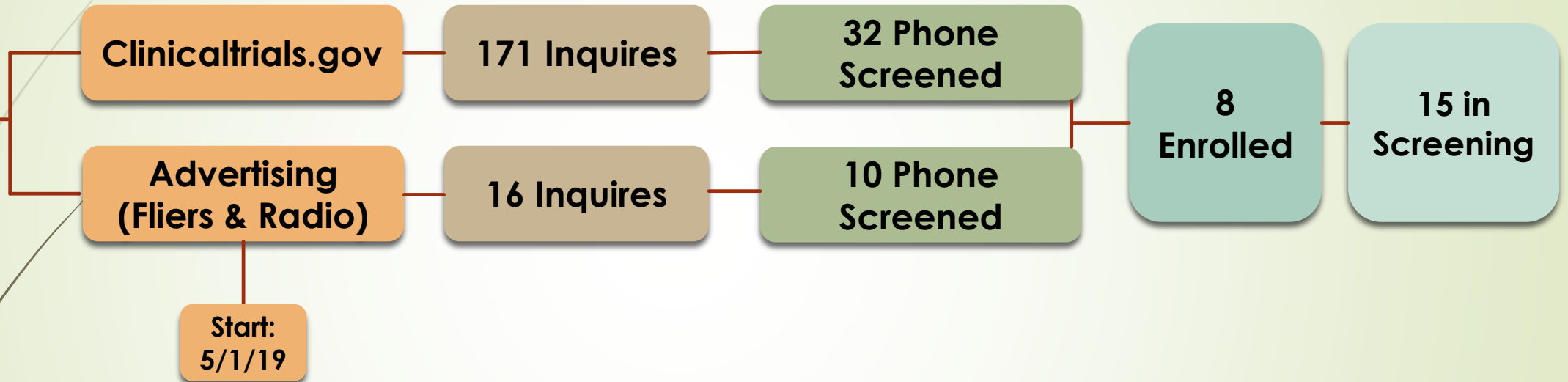
Bio-specimens



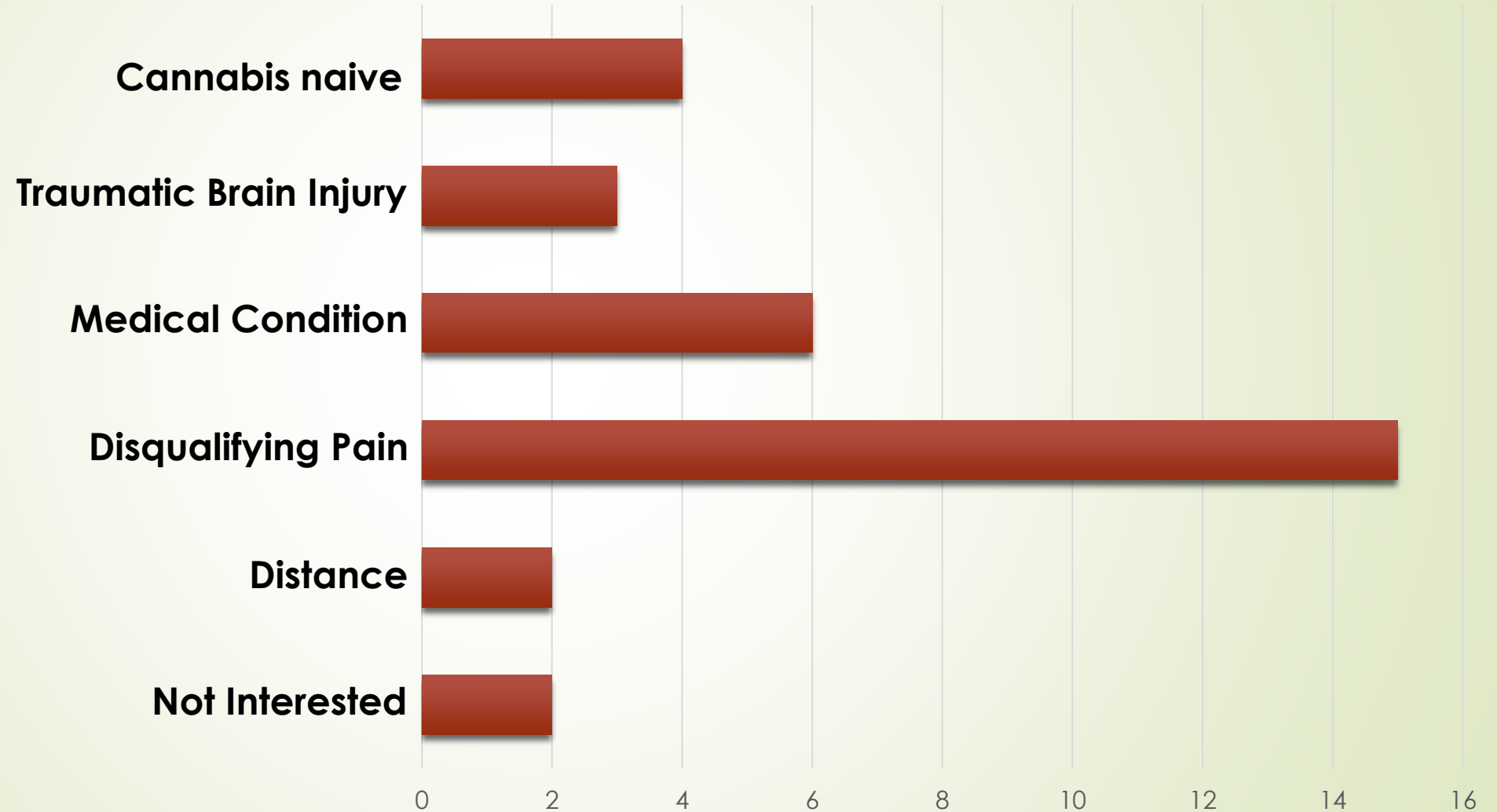
fMRI & MRS Scans

Recruitment Approaches

Efforts

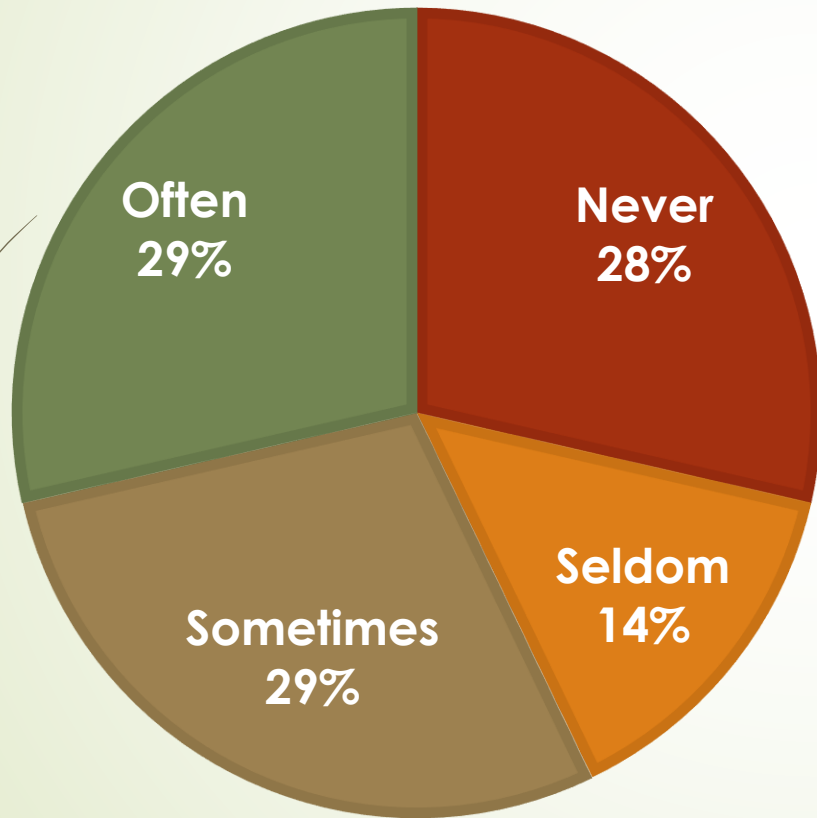


Reasons for Ineligibility

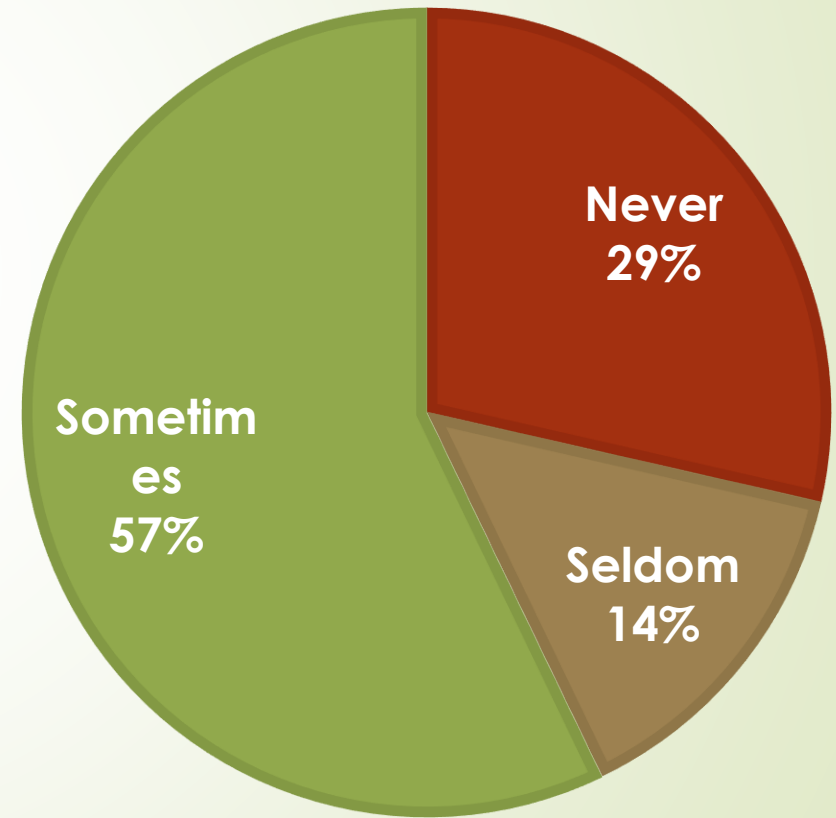


Opioid Use Factors

NEED HIGHER DOSE



IMPATIENT WITH DOCTOR



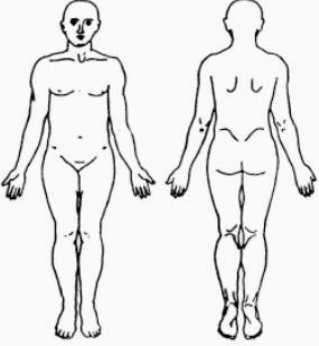
Pain Characteristics

- Average Pain Rating At 1st dosing visit = 4.1
- Worst Pain on over past 24 hours = 4.5
- Lowest Pain over past 24 hours = 2.3
- Average Duration of Pain in months = 90 (7.5yrs)
 - Range = 12 – 204 months (1 -17 yrs)
- Common Locations
 - Low Back
 - Hips & SI joints
 - Neck

McGill Pain Questionnaire

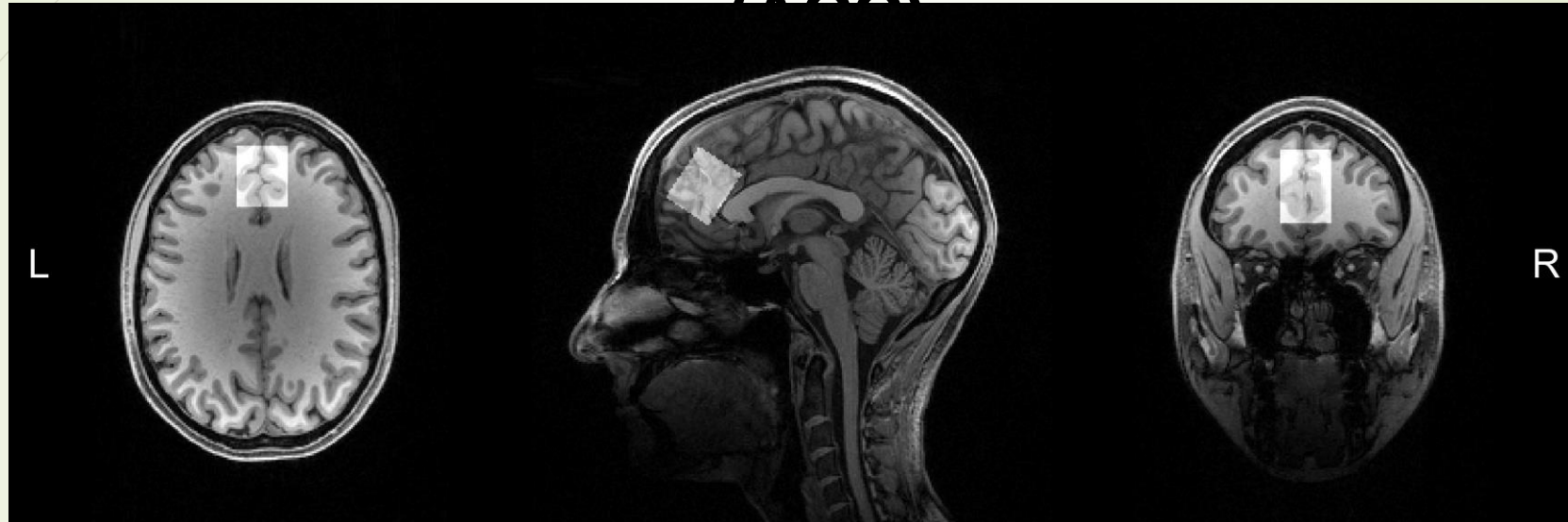
Patient's Name _____ Date _____ Time _____ am/pm

PRI: S _____ A _____ E _____ M _____ PRI(T) _____ PPI _____
 (1-10) (11-15) (16) (17-20) (1-20)

<table border="1" style="width: 100%; border-collapse: collapse;"> <tr><td>1 FLICKERING</td><td>11 TIRING</td></tr> <tr><td>QUIVERING</td><td>EXHAUSTING</td></tr> <tr><td>PULSING</td><td>12 SICKENING</td></tr> <tr><td>THROBBING</td><td>SUFFOCATING</td></tr> <tr><td>BEATING</td><td>13 FEARFUL</td></tr> <tr><td>POUNDING</td><td>FRIGHTFUL</td></tr> <tr><td>2 JUMPING</td><td>TERRIFYING</td></tr> <tr><td>FLASHING</td><td>14 PUNISHING</td></tr> <tr><td>SHOOTING</td><td>GRUELLING</td></tr> <tr><td>3 PRICKING</td><td>CRUEL</td></tr> <tr><td>BORING</td><td>VICIOUS</td></tr> <tr><td>DRILLING</td><td>KILLING</td></tr> <tr><td>STABBING</td><td>15 WRETCHED</td></tr> <tr><td>LANCINATING</td><td>BLINDING</td></tr> <tr><td>4 SHARP</td><td>16 ANNOYING</td></tr> <tr><td>CUTTING</td><td>TROUBLESOME</td></tr> <tr><td>LACERATING</td><td>MISERABLE</td></tr> <tr><td>5 PINCHING</td><td>INTENSE</td></tr> <tr><td>PRESSING</td><td>UNBEARABLE</td></tr> <tr><td>GNAWING</td><td>17 SPREADING</td></tr> <tr><td>CRAMPING</td><td>RADIATING</td></tr> <tr><td>CRUSHING</td><td>PENETRATING</td></tr> <tr><td>6 TUGGING</td><td>PIERCING</td></tr> <tr><td>PULLING</td><td>18 TIGHT</td></tr> <tr><td>WRENCHING</td><td>NUMB</td></tr> <tr><td>7 HOT</td><td>DRAWING</td></tr> <tr><td>BURNING</td><td>SQUEEZING</td></tr> <tr><td>SCALDING</td><td>TEARING</td></tr> <tr><td>SEARING</td><td>19 COOL</td></tr> <tr><td>8 TINGLING</td><td>COLD</td></tr> <tr><td>ITCHY</td><td>FREEZING</td></tr> <tr><td>SMARTING</td><td>20 NAGGING</td></tr> <tr><td>STINGING</td><td>NAUSEATING</td></tr> <tr><td>9 DULL</td><td>AGONIZING</td></tr> <tr><td>SORE</td><td>DREADFUL</td></tr> <tr><td>HURTING</td><td>TORTURING</td></tr> <tr><td>ACHING</td><td></td></tr> <tr><td>HEAVY</td><td>PPI</td></tr> <tr><td>10 TENDER</td><td>0 NO PAIN</td></tr> <tr><td>TAUT</td><td>1 MILD</td></tr> <tr><td>RASPING</td><td>2 DISCOMFORTING</td></tr> <tr><td>SPLITTING</td><td>3 DISTRESSING</td></tr> <tr><td></td><td>4 HORRIBLE</td></tr> <tr><td></td><td>5 EXCRUCIATING</td></tr> </table>	1 FLICKERING	11 TIRING	QUIVERING	EXHAUSTING	PULSING	12 SICKENING	THROBBING	SUFFOCATING	BEATING	13 FEARFUL	POUNDING	FRIGHTFUL	2 JUMPING	TERRIFYING	FLASHING	14 PUNISHING	SHOOTING	GRUELLING	3 PRICKING	CRUEL	BORING	VICIOUS	DRILLING	KILLING	STABBING	15 WRETCHED	LANCINATING	BLINDING	4 SHARP	16 ANNOYING	CUTTING	TROUBLESOME	LACERATING	MISERABLE	5 PINCHING	INTENSE	PRESSING	UNBEARABLE	GNAWING	17 SPREADING	CRAMPING	RADIATING	CRUSHING	PENETRATING	6 TUGGING	PIERCING	PULLING	18 TIGHT	WRENCHING	NUMB	7 HOT	DRAWING	BURNING	SQUEEZING	SCALDING	TEARING	SEARING	19 COOL	8 TINGLING	COLD	ITCHY	FREEZING	SMARTING	20 NAGGING	STINGING	NAUSEATING	9 DULL	AGONIZING	SORE	DREADFUL	HURTING	TORTURING	ACHING		HEAVY	PPI	10 TENDER	0 NO PAIN	TAUT	1 MILD	RASPING	2 DISCOMFORTING	SPLITTING	3 DISTRESSING		4 HORRIBLE		5 EXCRUCIATING	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>BRIEF MOMENTARY TRANSIENT</td> <td>RHYTHMIC PERIODIC INTERMITTENT</td> <td>CONTINUOUS STEADY CONSTANT</td> </tr> </table> <div style="text-align: center; margin: 20px 0;">  </div> <div style="text-align: center; margin: 10px 0;"> <div style="border: 1px solid black; padding: 2px; display: inline-block;">E = EXTERNAL</div> <div style="border: 1px solid black; padding: 2px; display: inline-block;">I = INTERNAL</div> </div> <div style="border: 1px solid black; height: 100px; margin-top: 20px;"> <p style="margin: 5px 5px 0 5px;">COMMENTS:</p> </div>	BRIEF MOMENTARY TRANSIENT	RHYTHMIC PERIODIC INTERMITTENT	CONTINUOUS STEADY CONSTANT
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Spectroscopy Methods

1H MRS Focused on Anterior Cingulate Cortex

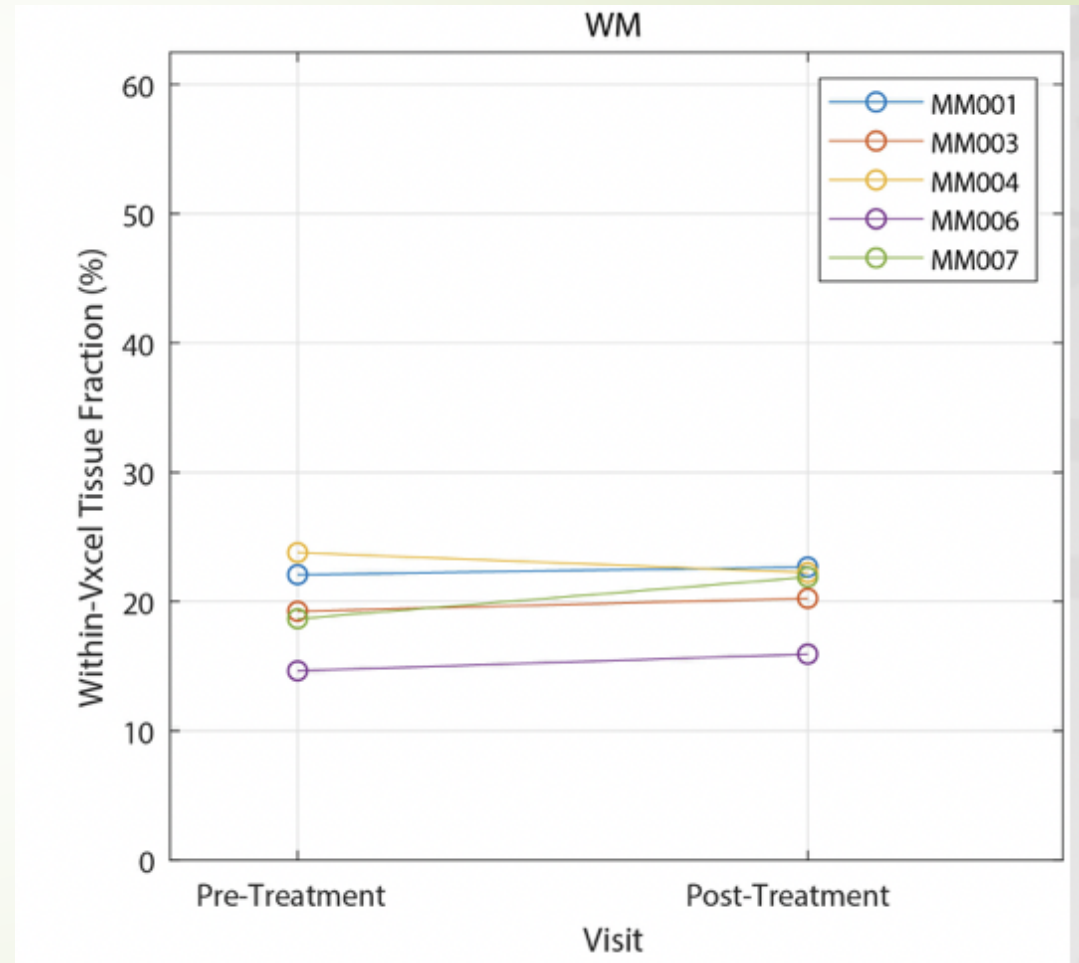
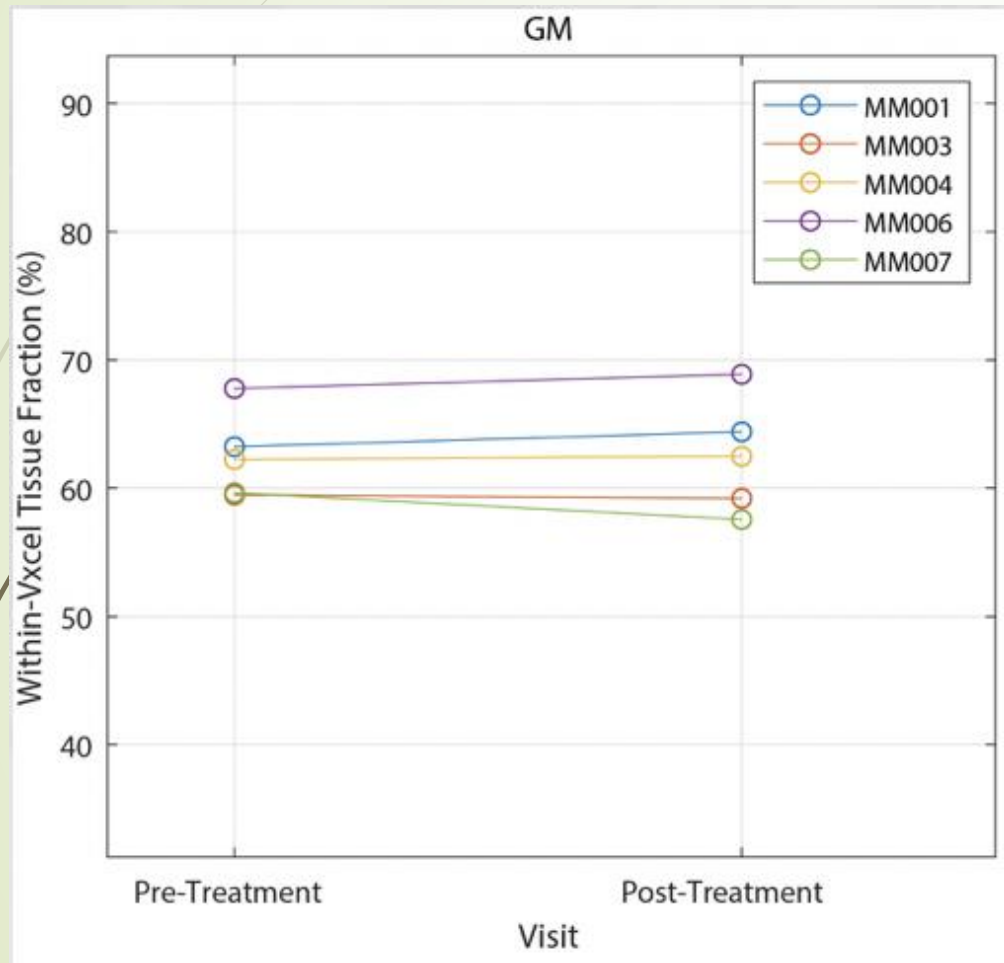


- **Two types of 1H MRS measurements performed:**

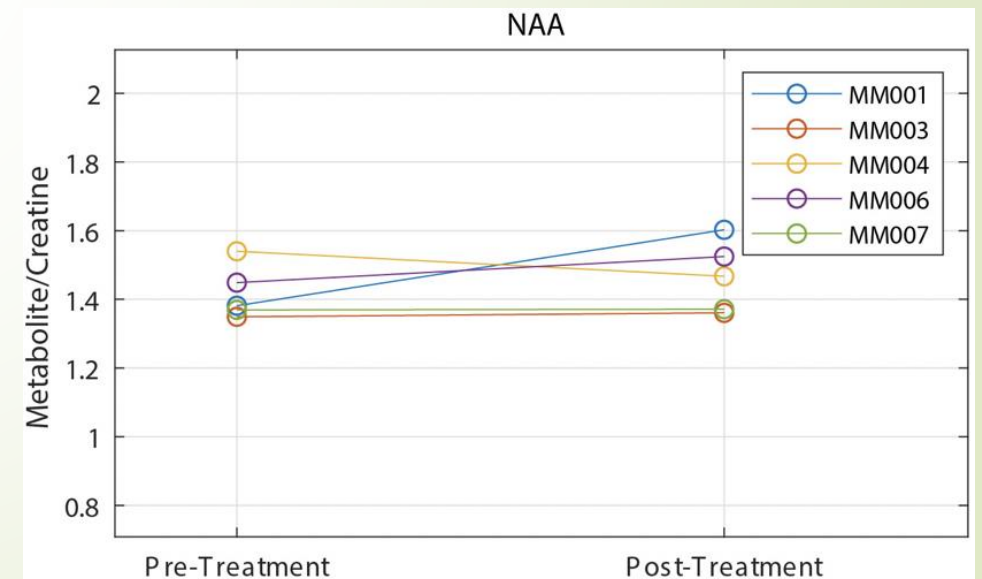
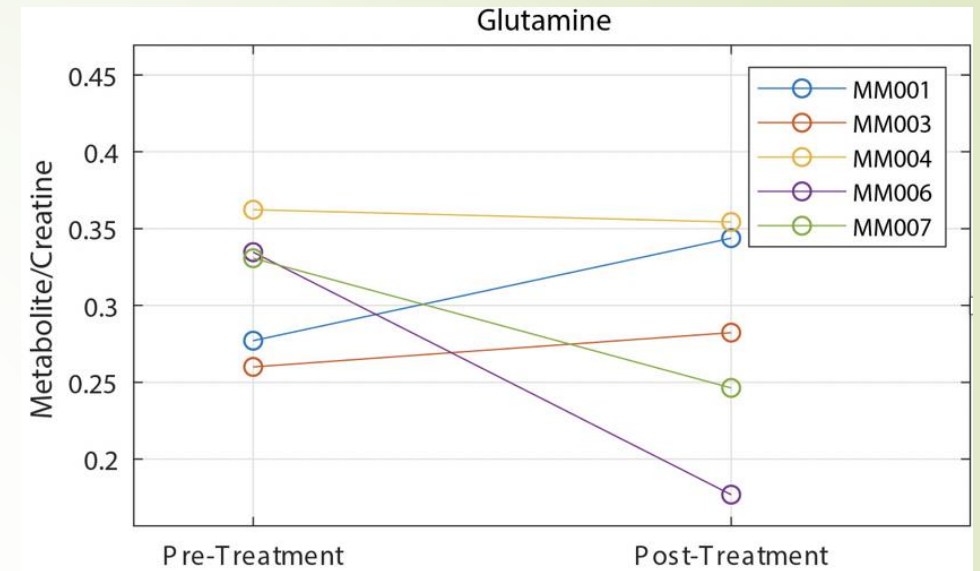
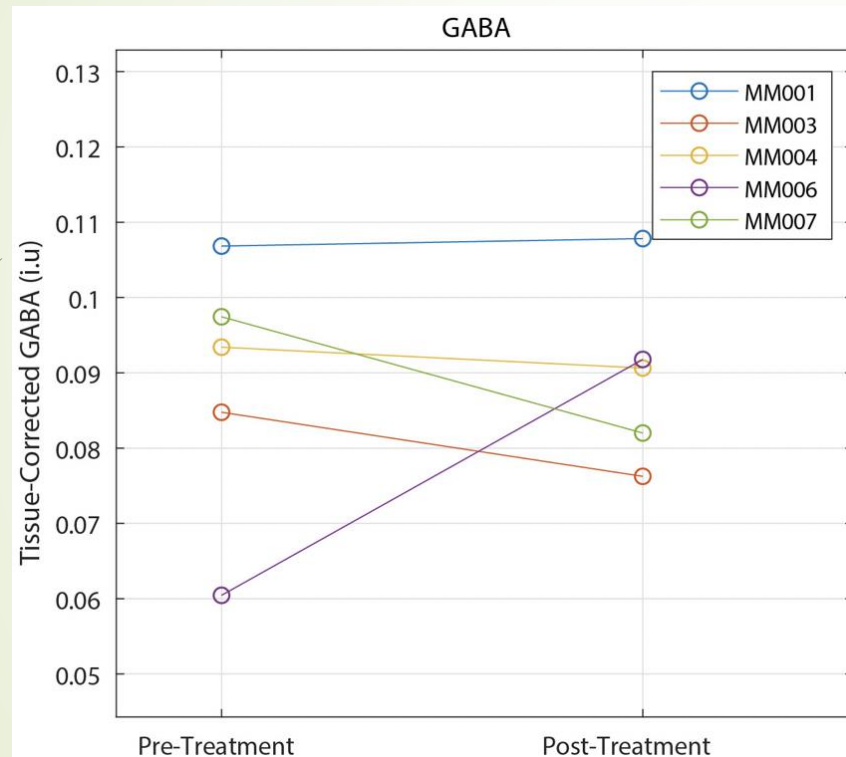
- J-edited 1H MRS (HERMES) for ACC GABA measures

- Two-dimensional (2D) J-resolved 1H MRS for measures of other ACC metabolites including glutamate, glutamine, NAA, *myo*-inositol, and choline-containing compounds

Stability of Tissue Composition



ACC Metabolite Measures: 2D J-resolved ^1H MRS



Assessment of Pressure Algometry

- **Assessed Usability of Two Different Pressure Algometers**
 - Digital – increasing pressure
 - Manual – steady pressure across time
- **Fifty-nine participants**
 - Half female, ages 19-70
 - Found that manual algometer is ok for pain threshold, but has a ceiling effect when measuring tolerance
 - Participants tolerate objective pain measures in research protocols



Objective Pain Measurement – Pressure Algometer in MJ Sample

- **Average Pre-Dose Pain Threshold = 10.03 (4.25) lbf**
 - **Range = 4.78 – 19.49 lbf of Pressure**
- **Average Post-Dose Pain Threshold = 10.57 (5.09) lbf**
 - **Range = 5.48 – 22.01 lbf of Pressure**
- **Increase in Pain Threshold Post -Dose**

